REMARKS

CLAIM AMENDMENTS

Claim 1 has been amended to incorporate subject matter from claim 4 and to delete the phrase "agonists thereof." Claims 23-28 have also been amended to incorporate subject matter from claim 4 and to delete the phrase "agonists thereof, and combinations thereof." The amendments to claims 1 and 23-28 are made without prejudice to claim the deleted subject matter in a later-filed application.

With the amendment to claim 1, claims 3, 4, and 15 have been canceled as redundant.

Claim 24 has been amended to delete the word "maintaining." Support for the change to claim 24 is found in the specification at, *inter alia*, page 6, lines 20-21, and page 42, lines 19-20.

No new matter has been added to the application with the claim amendments set forth herein.

PRIORITY

Applicants acknowledge that the parent applications of the instant application disclose and claim VIP agonists and analogs, and thus, the priority claim for VIP agonists and analogs in this application dates back to the October 28, 1997, filing date of the earliest filed parent application, U.S. Patent Application Serial No. 09/595,057.

CLAIM REJECTION – 35 U.S.C. § 112, SECOND PARAGRAPH

Claims 1-15 and 20-28 stand rejected under 35 U.S.C. § 112, second paragraph, as indefinite. Specifically, the Examiner notes that claims 1 and 23-28 recite non-elected subject matter, claim 2-15 and 20-22 depend from a rejected claim base, and claim 24 includes indefinite language.

As set forth above, claims 1 and 23-28 have been amended to delete the rejected subject matter and claim 24 has been amended to clarify the meaning of the claim.

In light of the changes made to the claims, applicants respectfully request reconsideration and withdrawal of this rejection.

CLAIM REJECTION – 35 U.S.C. § 112, FIRST PARAGRAPH

Claims 25 and 26 stand rejected under 35 U.S.C. § 112, first paragraph, as nonenabling. This rejection is respectfully traversed.

35 U.S.C. § 112, first paragraph, reads as follows:

> *The specification shall* contain a written description of the invention, *and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same,* and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The purpose of the enablement requirement is to assure that inventors provide sufficient information about the claimed invention that a person of skill in the field of the invention can make and use it without undue experimentation, relying on the specification and the knowledge in the art. *Scripps Clinic & Research Foundation v. Genentech, Inc.*, 927 F.2d 1565, 18 USPQ2d 1896 (Fed. Cir. 1991). The enablement requirement is met if the description enables any mode of making and using the claimed invention. *Engel Industries, Inc. v. Lockformer Co.*, 946 F.2d 1528, 20 USPQ2d 1300 (Fed. Cir. 1991). The Federal Circuit has explained that the question of undue experimentation is not a single, simple factual determination, but rather, it is a conclusion that is reached by weighing many factual considerations. *In re Wands,* 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988) (The key word is "undue," not "experimentation.").

In *In re Wands,* the Federal Circuit set forth eight factors to consider when determining whether a disclosure would require undue experimentation, they are: (1) the quantity of experimentation necessary; (2) the amount of direction or guidance presented; (3) the presence or absence of working examples; (4) the nature of the invention; (5) the state of the prior art; (6) the relative skill of those in the art; (7) the predictability or unpredictability of the art; and (8) the breadth of the claims. The Federal Circuit has, on more than one occasion, cautioned that the *Wands* factors are illustrative and not mandatory and that all of the factors need not be reviewed when determining whether a disclosure is enabling. *Enzo Biochem., Inc. v. Calgene, Inc.*, 188 F.3d 1362, 52 USPQ2d 1129 (Fed. Cir. 1999), citing, *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991), *cert. denied,* 502 U.S. 856 (1989).

Applying the *Wands* factors, the Examiner takes the position that the claimed invention is not enabling. The following discussion will demonstrate the errors in the Examiner's *Wands* factor analysis and why the claimed invention is legally enabling. The following outlines analyzes the eight *Wands* factors as enumerated by the Federal Circuit; the Examiner's *Wands* factor analysis sets forth only six of the eight *Wands* factors. For purposes of clarity, the *Wands* factors are discussed in the order presented by the Examiner in the Office Action.

1. **THE NATURE OF THE INVENTION:**

The Examiner characterizes the nature of the invention as "a pharmaceutical for the treatment of vaginal atrophy and vaginal pain during intercourse, or to keep from happening" (Office Action, p.4, discussion of *Wands* factor no. 1). As the foregoing discussion will demonstrate, the Examiner's statement of the nature of the invention is not an accurate statement.

Guidance on interpreting the "nature of the invention" *Wands* factor is set forth at MPEP § 2164.05(a). There, it explains that the nature of the invention, i.e., the subject matter to which the claimed invention pertains, is the backdrop to determine the state of the art and the level of skill possessed by one skilled in the art (MPEP, 8th ed., Rev. Feb. 1, 2003, p. 2100-184). The MPEP explains that the pertinent art should be defined in terms of the *problem to be solved* rather than in terms of the technology area, industry, trade, etc. for which the invention is used (page 2100-185, ¶ 2).

The problem to be solved by the claimed invention is the treatment of female sexual dysfunction (*see*, spec., p.6, ll. 9-10); thus, contrary to the Examiner's assertion, the nature of the invention is ***not*** "a pharmaceutical treatment for the treatment of vaginal atrophy and pain during sexual intercourse." The Examiner's characterization of the nature of the invention relates to the method by which the physical manifestations of female sexual dysfunction, i.e., vaginal atrophy and pain during intercourse, are resolved; this is ***not*** the nature of the invention, but rather, it is the method by which the nature of the invention, i.e., the problem to be solved, is addressed.

With the nature of the invention properly identified, the references cited in the IDS, show that at the time the application was filed, the ordinary artisan was addressing the problems of female sexual dysfunction and attempting to find ways to improve female sexual responsiveness as well as the physical manifestations that lead to problems in female sexual behavior. Based on this showing, applicants submit that the nature of the invention, i.e., the treatment of sexual dysfunction, enables the recitation in claims 25 and 26, i.e., the treatment of vaginal atrophy and pain during sexual intercourse.

2. **THE BREADTH OF THE CLAIMS:**

For this *Wands* factor, the Examiner states that "applicants are claiming a composition that is an agent for 'preventing' vaginal atrophy and vaginal pain during intercourse" (Office Action, p.4, discussion of *Wands* factor no. 2). The Examiner does not specify that the claims are overly broad in this respect, and thus, it appears that the Examiner does not have any objection to the

breadth of the claims. Notwithstanding the foregoing, applicants note that *the claims actually recite that the composition is vasoactive intestinal polypeptide ("VIP").*

Turning again to the MPEP for guidance on what the Federal Circuit expects from the breadth of the claims *Wands* factor, the MPEP at section 2164.08 explains that when analyzing the enabling scope of a claim, the teachings of the specification must not be ignored because claims are to be given their broadest reasonable interpretation consistent with the specification. To illustrate the importance of this requirement, the MPEP quotes the following statement from *In re Goffe,* 542 F.2d 564, 567, 191 USPQ 429, 431 (CCPA 1976):

> [T]o provide effective incentives, claims must adequately protect inventors. To demand that the first to disclose shall limit his claims to what he has found will work or to materials which meet the guidelines specified for "preferred" materials in a process such as the one herein involved would not serve the constitutional purpose of promoting progress in the useful arts. MPEP § 2164.08, p. 2100-191, col. 2, ¶ 1.

With respect to the issue of undisclosed species, this issue primarily comes into play when an inventor is claiming a new species of plant, animal etc. for which the ordinary artisan would have no knowledge prior to the disclosure in the patent document at issue. Referring to the example given in the MPEP at section 2164.08, in *Amgen v. Chugai,* the Federal Circuit held that Amgen could not generically claim all analogs of the newly cloned EPO gene because only a few EPO genes were disclosed in the Amgen patent and there might be other genetic sequences that code for EPO-type products. MPEP § 2164.08, p. 2100-192, col. 1, ¶ 1, citing, *Amgen v. Chugai Pharmaceutical Co.,* 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir.), *cert. denied,* 502 U.S. 856 (1991).

In the instant case, applicants are claiming a method of preventing vaginal atrophy or pain during sexual intercourse by administering VIP. Human VIP is disclosed in the specification at page 14 with SEQ. ID NO. 1. There, it is stated that VIP from other species are known to exhibit homology to human VIP and therefore expected to exhibit VIP agonistic and/or antagonistic activity (spec., p.14, ll. 8-11). Because the specification expressly identifies the sequence for VIP with one single sequence, it is difficult to argue that the breadth of claims 25 and 26 is overly broad. In light of the foregoing, applicants submit that the breadth of claims 25 and 26 is fully enabled by the disclosure in the specification.

3. THE STATE OF THE PRIOR ART:

The Examiner asserts that the state of the art "does not teach the absolute prevention of vaginal atrophy and vaginal pain during sexual intercourse, merely that the symptoms of the dysfunctions, such as muscle tone and tissue health, and dyspareunia [citations omitted] may be treated. (Office Action, p.4, discussion of *Wands* factor no. 3).

As will be explained in detail *infra*, the state of the art is used to determine the amount of detail that must be provided in the specification in order for it to be enabling; state of the art that is contradictory to a claimed invention will only render an invention non-enabling if the application fails to provide enough detail to overcome the deficiencies in the prior art. In the instant case, the specification provides sufficient detail for the ordinary artisan to practice the invention as recited in claims 25 and 26.

MPEP § 2164.05(a) explains that the state of the prior art is what one skilled in the art would have known at the time the application was filed about the subject matter to which the claimed invention pertains. MPEP § 2164.05(a), p. 2100-184, col. 2, ¶ 2. The state of the prior art provides evidence for the degree of predictability in the art and is related to the amount of direction or guidance needed in the specification as filed to meet the enablement requirement. MPEP § 2164.05(a), p. 2100-184, col. 2, ¶ 3. The state of the prior art is also related to the need for working examples in the specification. *Id.* MPEP § 2164.03 explains that the amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability of the art. MPEP § 2164.03, p. 2100-182, col. 1, ¶ 1. Thus, when a great deal is known in the prior art about the nature of the invention and the invention is in a predictable art, then less information on how to make and use the invention is required in the specification. *Id.* By contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, then in order for the specification to be enabling, it must disclose more detail on how to make and use the invention. *Id.*

A review of the specification (pages 1-6) of the instant application and the art cited in the IDS of November 21, 2001, reveals that quite a lot of research has been undertaken on the treatment of female sexual dysfunction, albeit not with VIPs, as well as on the use of VIP for the treatment of various physiological disorders, that is, other than female sexual dysfunction. In light of the state of the art of female sexual dysfunction and of the use of VIP generally, a great deal of guidance is not required in order to provide a sufficient disclosure to enable the ordinary artisan to make and use the invention. Notwithstanding the foregoing, the specification does provides over five pages of background (pp. 1-6); close to five pages of definitions (pp. 8-12); approximately 12

pages of examples of VIPs (pp. 12- 24); over one page of a discussion of the synthesis of VIPs (pp. 24-25); over 8 pages of examples of secondary agents that may be administered with the disclosed VIPs (pp. 25-33); approximately ten pages describing various formulations, modes of administration, and disorders that may be treated by the claimed formulations (pp. 33-43); and lastly, ten examples. The total length of the specification is 44 pages, not counting the claims.

In keeping with the requirements of the "prior art" *Wands* factor, the applicants have provided a disclosure that would satisfy even the most obscure state of the art. Because the state of the art of female sexual dysfunction and of VIPs generally has been previously explored, applicants submit that the ordinary artisan would readily be able to make and use the invention of claims 25 and 26 by reading through the detailed specification. That the state of the art does not teach the absolute prevention of vaginal atrophy and vaginal pain during sexual intercourse is not a surprise, as the prevention of vaginal atrophy and vaginal pain during sexual intercourse is one aspect of the present invention that is first disclosed with the instant application. In light of the state of the art at the time of the invention, applicants submit that claims 25 and 26 are fully enabled by the detailed disclosure of the invention as set forth in the specification.

4. THE PREDICTABILITY OR UNPREDICTABILITY OF THE ART:

The Examiner contends that the invention as claimed in claims 25 and 26 is highly unpredictable given the current state of the art (Office Action, p.4, discussion of *Wands* factor no. 4).

As will be explained *infra*, the unpredictability *Wands* factor relates to the number of species that must be disclosed in an application in order for a claim to be enabled. In the instant case, the limitation of claims 25 and 26 to one species, i.e., VIP, demonstrates that these two claims must be fully enabled even in an unpredictable art.

MPEP § 2164.03 explains that the "predictability or lack thereof" in the art refers to the ability of one skilled in the art to extrapolate the disclosed or known results to the claimed invention. MPEP § 2164.03, p. 2100-182, col. 1, ¶ 2. In other words, if one skilled in the art can readily anticipate the effect of a change within the subject matter (such as a newly found species) to which the claimed invention pertains, then there is predictability in the art. *Id.* By contrast, if one skilled in the art cannot readily anticipate the effect of a change within the subject matter to which that claimed invention pertains, then there is a lack of predictability in the art. *Id.* With respect to the amount of disclosure required in an unpredictable art, the MPEP notes that even in

unpredictable arts, a disclosure of every operable species is not required, but more than one will usually be necessary. MPEP § 2164.03, p. 2100-182, col. 2, ¶ 2.

In the instant case, applicants disclose many VIP agonists and analogs VIP as species that may be useful to treat vaginal atrophy and pain during sexual intercourse, but as noted above, claims 25 and 26 only claim one species – endogenous VIP. Accordingly, even with an unpredictable art, the recitation of a single species in claims 25 and 26, there is no question that these claims are fully enabled even in view of any unpredictability inherent in the art of treatment of female sexual dysfunction.

5. THE AMOUNT OF DIRECTION OR GUIDANCE PRESENTED:

The Examiner asserts that the specification lacks working examples or guidance for the use of VIP for the prevention of symptoms (Office Action, p.4, discussion of *Wands* factor no. 5).

Applicants submit that the results of disclosed experiments are irrelevant to the "amount of direction or guidance" *Wands* factor; the following discussion explains why this is the case.

MPEP § 2164.03 explains that the "amount of guidance or direction" refers to the information in the application, as originally filed, that teaches exactly ***how to make or use*** the invention. MPEP § 2164.03, p. 2100-182, col. 1, ¶ 1). Contrary to the Examiner's position, the MPEP does ***not*** require that the application present "results" derived from the invention; all that is required is that the ordinary artisan, upon reading the specification, knows *how to make and use* the invention. This important provision of the enablement requirement is also emphasized at MPEP § 2164.04, which provides Examiners with guidance on preparing enablement rejections. *See,* MPEP § 2164.04, p. 2100-183, col. 2, first five lines, where it is stated that "[t]he language should focus on those factors, reasons, and evidence that lead the examiner to conclude that the specification fails to teach how to make and use the claimed invention without undue experimentation..."

In response to the Examiner's assertion that the application lacks direction or guidance, applicants respectfully direct the Examiner's attention to page 33, lines 13-24, of the specification where it is explained that the formulations of the present invention are applied to the vulvar region and/or by vaginal drug administration. Suitable formulations are described at pages 33-38, modes of administration are described at pages 38-41, and patients that may benefit from the claimed formulations are described at pages 41-42. Because the ordinary artisan would readily understand how to use the claimed invention for the prevention of vaginal atrophy and pain during sexual intercourse through a reading of the disclosure, it follows that the disclosure provides adequate direction and guidance for the ordinary artisan to prepare the claimed formulations and to instruct the patient suffering from the vaginal atrophy and pain during sexual intercourse on how to apply

the formulations. Accordingly, applicants submit that the specification provides sufficient direction and guidance to enable claims 25 and 26.

6. THE QUANTITY OF EXPERIMENTATION:

The Examiner contends that the practice of the claimed invention requires undue and unpredictable experimentation. Again, applicants note that claims 25 and 26 recite only one species, VIP. To say that claims 25 and 26 require undue experimentation when they are directed to only one species is a curious statement indeed.

At MPEP § 2164.06, the MPEP quotes the following statement from *In re Colianni*: "An extended period of experimentation may not be undue if the skilled artisan is given sufficient direction or guidance." MPEP § 2164.06, quoting, *In re Colianni,* 561 F.2d 220, 224, 195 USPQ 150, 153 (CCPA 1977). Applicants demonstrated that the instant specification provides sufficient direction and guidance in the discussion set forth immediately above at No. 5.
Because the specification provides sufficient direction and guidance for the ordinary artisan to practice the invention of claims 25 and 26, which is only directed to one species of vasoactive agents, i.e., endogenous VIP, it follows that there can be no plausible assertion that these two claims are subject to undue experimentation.

7. THE RELATIVE SKILL OF THOSE IN THE ART:

The Examiner provides no commentary on this *Wands* factor. Applicants are interpreting the Examiner's silence on this factor to be an acknowledgement that the application is enabling to persons skilled in the art of sexual research on female subjects. *See,* MPEP § 2164.05(b) for a discussion of the requirements for the *Wands* factor relating to the relative skill of those in the art.

8. THE PRESENCE OR ABSENCE OF WORKING EXAMPLES:

The Examiner addressed this *Wands* factor under the sixth *Wands* factor set forth above, i.e., the amount of guidance or direction presented.

***WANDS* FACTOR CONCLUSION**

The foregoing analysis demonstrates that the invention as recited in claims 25 and 26 meet all of the requirements of the *Wands* factors; accordingly, it follows that claims 25 and 26 are fully enabled by the disclosure. Accordingly, applicants respectfully request reconsideration and withdrawal of this rejection.

CLAIM REJECTION – 35 U.S.C. § 102(e)

Claims 1, 2, 6, 11, 12, and 14 stand rejected under 35 U.S.C. § 102(e) as anticipated by U.S. Patent No. 6,031,002 to Wysor et al. ("Wysor et al."). This rejection is respectfully traversed.

With the amendment to claim 1 to include subject matter from claim 4, this rejection is rendered moot.

CLAIM REJECTION UNDER 35 U.S.C. § 103(a) OVER OTTENSEN ET AL. IN THE PAPER "PEPTIDES"

Claims 1, 2, 6-15, and 23-28 stand rejected under 35 U.S.C. § 103(a) as obvious over Ottensen et al., PEPTIDES 8(5):797-800 (1987). This rejection is respectfully traversed.

With the amendment to claim 1 to include subject matter from claim 4, this rejection is rendered moot.

CLAIM REJECTION UNDER 35 U.S.C. § 103(a) OVER WYSOR ET AL. AND OTTENSEN ET AL. IN THE PAPER "REGULATORY PEPTIDES"

Claims 1-15 and 23-28 stand rejected under 35 U.S.C. § 103(a) as obvious over Wysor et al. in view of Wysor et al. and Ottensen et al., REGULATORY PEPTIDES 11:83-92 (1985). This rejection is respectfully traversed.

As noted by the Examiner on page 6, item 9, of the Office Action, Wysor et al. does not teach or suggest a combination of VIP and a steroid for the treatment of female sexual dysfunction. The Examiner cited Ottensen et al. for the teaching that steroids affect VIP.

The Examiner's hypothetical combination of Wysor et al. in view of Ottensen et al. does not render the claimed invention obvious because Ottensen et al. only teaches that estrogen or progesterone influence the motor effects of VIP and does ***not*** teach or suggest that androgens have the same influence on VIP as estrogen or progesterone. Indeed, nowhere in Ottensen et al. are androgens even mentioned.

Because Wysor et al. in view of Ottensen et al. do not teach or suggest that androgens are able to mediate the motor effects of VIP, it follows that the hypothetical combination of Wysor et al. in view of Ottensen et al. does not render the claimed invention obvious. Accordingly, applicants respectfully request reconsideration and withdrawal of this rejection.

CLAIM OBJECTIONS

With the amendment to claim 1, the Examiner's objection to the language of claim 1 is rendered moot.

PRIOR ART NOT RELIED UPON

Applicants have reviewed the prior art cited but not relied upon and acknowledge that the cited art is sufficiently removed from the claimed invention so as to not warrant application against the claimed invention.

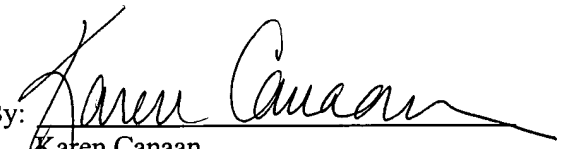
CONCLUSION

The *prima facie* case is a procedural tool which, as used in patent examination, means not only that the evidence of the prior art would reasonably allow the conclusion the Examiner seeks, but also that the prior art compels such a conclusion if the applicant produces no evidence or argument to rebut it. *In re Spada,* 911 F.2d 705 (Fed. Cir. 1990). If examination at the initial stage does not produce a *prima facie* case of unpatentability, then without more, the applicant is entitled to a grant of the patent. *In re Oetiker,* 977 F.2d 1443 (Fed. Cir. 1992).

As each of the Examiner's rejections have been addressed and overcome with this paper, applicants respectfully submit that they are entitled to a patent grant for the claimed invention. *See, In re Oetiker, supra.*

Should the Examiner have any questions concerning this response, she is welcome to telephone the undersigned attorney at (650) 330-4913 or at canaan@reedpatent.com.

Respectfully submitted,

By: 
Karen Canaan
Registration No. 42,382

REED & EBERLE LLP
800 Menlo Avenue, Suite 210
Menlo Park, California 94025
(650) 330-0900 Telephone
(650) 330-0980 Facsimile